UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,783	02/28/2005	Richard Keith	100822-1P US	8524

22466 7590 06/27/2006

ASTRA ZENECA PHARMACEUTICALS LP
GLOBAL INTELLECTUAL PROPERTY
1800 CONCORD PIKE
WILMINGTON, DE 19850-5437

EXAMINER	
OLSON, ERIC	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 06/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/525,783	KEITH, RICHARD	
	Examiner	Art Unit	
	Eric S. Olson	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-23* is/are pending in the application.

4a) Of the above claim(s) *23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13,14 and 16-22* is/are rejected.

7)☒ Claim(s) *15* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date ~~September 1, 2005~~ 02-28-05
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

This application is a national stage application of PCT international publication PCT/SE03/01352, filed September 1, 2003, which claims benefit of international application SE 0202598-9, filed September 2, 2002. Claims 13-23 are pending in this application and examined on the merits herein. Applicant's preliminary amendment submitted May 30, 2006 is acknowledged wherein claim 13 is amended, claim 17 is cancelled, and new claims 22-23 are introduced.

Response to Restriction/Election

Applicant's election with traverse of the invention of group I, claims 13-22 in part, submitted May 30, 2006, is acknowledged.

Applicant's traversal with respect to the alleged lack of unity between groups I and II has been considered and not found to be convincing. The traversal is on the grounds that the alleged synergistic benefit provided by the combination of two pharmaceutical agents, a statin and an α7-nAChR agonist, constitutes a special technical feature which distinguishes the claimed invention from the prior art, and that a combination of a statin with one of the spiro compounds of group I has unity of invention with a combination of a statin and one of the amides of group II. However, Applicant's claimed invention is not merely a combination of a statin with an α7-nAChR agonist of indeterminate structure, or even one defined only by a generic quinuclidine core structure. Rather, Applicant claims combinations comprising compounds of certain well-defined structures. The fact that these compounds are disclosed as possessing α7-

nAChR agonist activity does not constitute a special technical feature. Furthermore, as statins are already well known in the prior art, the statin used in the claimed combination does not constitute a special technical feature. As already stated in the previous office action, these two classes of molecules are recognized in the art to constitute two separate core structures as demonstrated by, for example, International applications WO2005/030778 and WO2005/042538, and US patent applications 11/089553 and 10/731565. (All cited or included with PTO-892 from the previous action) In all of these references, compounds from either group I or group II are disclosed separately. None of these references disclose both quinuclidine amides and quinuclidine spiro compounds together in the same reference. The prior art does not disclose these two classes of compounds as being a discrete group of related structures expected to possess any special activity which sets them uniquely apart from the prior art.

Thus neither the combination of two pharmaceutical agents, the presence of a statin, nor the presence of a quinuclidine core structure constitutes a special technical feature which sets the invention apart from the prior art. Rather, any special technical feature is limited to the disclosure of certain specific novel pharmaceutical compounds not known in the prior art to be useful for the treatment of the various claimed disorders.

Furthermore, the traversal is additionally on the ground that the Office has not applied the same standard of unity of invention as the International Preliminary Examination Authority. This argument is also not found persuasive. The examiner herein is evaluating unity of invention in the instant application for the first time in the national stage. The examiner herein is not bound by international stage prosecution.

Further, note in this regard that international prosecution was not handled in the US, but in the Swedish Patent Office, as noted in the international search report.

Therefore, groups I and II fail to meet PCT Rule 13.2 since they do not relate to a single general inventive concept. Thus the requirement for restriction is deemed proper and made FINAL. Claim 23 is withdrawn from consideration as being directed to non-elected subject matter. Note that the species, **N-(1-azabicyclo[2.2.2]oct-3-yl)[E-3-(2-thienyl)propenamide]**, appearing in claims 15 and 21, is also withdrawn as belonging to non-elected group II.

Applicant's provisional election of the single species of the combination of rosuvastatin and spiro[1-azabicyclo[2.2.2]octane-3,5'-oxizolidine]-2'-one is not relevant to the prosecution as an election of species was not required.

Claim Rejections – 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 17-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of using a combination comprising a statin and one of the disclosed α7-nAChR agonists to treat Alzheimer's disease and Parkinson's disease, does not reasonably provide enablement for a method of treating other diseases such as anxiety, schizophrenia, depression, Tourette's syndrome, or cessation of smoking. The specification does not enable any person skilled in the art to

which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The Applicant's attention is drawn to *In re Wands*, 8 USPQ2d 1400 (CAFC1988) at 1404 where the court set forth eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:
(1) The nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Nature of the invention: The claimed invention is a method of using a combination comprising a statin and an α7-nAChR agonist for the treatment of one of a number of diseases.

The state of the prior art: Statins are well known in the prior art to be useful for the treatment of Alzheimer's disease, and possibly other neurodegenerative diseases. (US patent 6274603, cited in PTO-892) Statins are not known to be useful, alone or in combination, for the treatment of any disease other than neurodegenerative diseases and hyperlipidemia. In particular, statins are not known to be useful for the treatment of cognitive or attention disorders, anxiety, depression, smoking cessation, schizophrenia, or Tourette's syndrome.

It has been speculated in the prior art that α7-nAChR receptor agonists could provide a neuroprotective effect. Additionally, US patent 6110914 (Reference cited in

PTO-1449) discloses a number of such agonists, including many of those mentioned in instant claim 14, which are said to be useful for the treatment of a number of disorders including Alzheimer's disease, attention deficit, Parkinson's disease, anxiety, schizophrenia, Tourette's syndrome, and smoking cessation. The prior art discloses no experimental data which would shed any light on the actual efficacy of α7-nAChR agonists in general for the treatment of disease, so extrapolating from this data to predict the therapeutic activity of any other compound is impossible.

A skilled practitioner of the medical or pharmacological arts would be motivated to combine and co-administer two substances either because both substances are useful for administration to the same patient population, or because one substance is useful as a pharmaceutically acceptable adjuvant, excipient, binder, solubilizing agent, or counterion for the other. However, the usual practice in the art is to use for this purpose compounds which are more or less biologically inactive, such as starches and polyethylene glycols, rather than compounds such as statins which possess an additional biological activity unrelated to the desired therapeutic effect.

The relative skill of those in the art: The relative skill of those in the art is high.

The predictability or unpredictability of the art: While statins are well known as therapeutic agents for the treatment of hyperlipidemia and Alzheimer's disease, they are not known in the prior art to be useful for the treatment of other diseases, particularly attention disorders, anxiety, depression, Tourette's syndrome, schizophrenia, or smoking cessation. These diseases are not known to have any correlation with ApoE

levels, cholesterol levels, or hyperlipidemia. Thus the results of any therapeutic regimen using them for this purpose would be unpredictable at best.

There exists no completely reliable animal model for Alzheimer's disease which can predictable assess the effectiveness of a particular therapy against this disease. (p. 12, lines 9-21) Thus the effectiveness of a particular therapy cannot be predicted based on experiments in a single animal model. For example, the effectiveness of statins against Alzheimer's disease was not discovered by experiments performed in an animal model but rather by analysis of epidemiological data gathered from human subjects already prescribed statins to treat hyperlipidemia.

The Breadth of the claims: A large number of specific α7-nAChR agonists are recited in instant claims 14 and 23 as being useful in the claimed combinations. A number of diseases are claimed as being treatable using the claimed combination. These diseases are related only in that they are all believed to involve insufficient activation of the α7-nAChR receptor.

The amount of direction or guidance presented: A significant number of specific α7-nAChR agonists are recited in the specification and in instant claims 14 and 23. These compounds are alleged to be α7-nAChR agonists, but no specific binding affinities or other data are given. The instant specification also provides a theory as to the method of operation of the claimed compositions, (p. 2 line 30 – p. 3 line 4) and suggests possible experiments which could be done to determine the activity of a particular combination as a therapeutic agent for the treatment of Alzheimer's disease.

No guidance is given as to suitable animal models for attention disorders, anxiety, depression, Tourette's syndrome, schizophrenia, or smoking cessation.

The presence or absence of working examples: There are no working examples presented in the applicant's specification.

Note that lack of working examples is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art such as the treatment of disease with α7-nAChR agonists. See MPEP 2164.

The quantity of experimentation necessary: Merely possessing two compounds does not enable one skilled in the art to produce a combination of the two compounds unless the combination is known to possess a utility which would motivation one of skill in the art to produce it. Thus, in order to practice the claimed invention, one skilled in the art would first have to determine which combinations possess any useful therapeutic properties. This would require that one skilled in the art test a representative sample of the combinations described in the specification, to determine their therapeutic effectiveness and biological properties. The existing literature does not identify any general method by which the usefulness of α7-nAChR agonists can be evaluated other than by synthesizing and testing each one. One skilled in the art would also be forced to test every molecule disclosed in the specification *in vivo* in order to determine which possess the greatest agonist activity, as no specific IC50 values or other therapeutic properties are given by which one skilled in the art could determine which of the recited compounds are the best drug candidates.

In order to practice the invention for the treatment of diseases other than Alzheimer's and Parkinson's disease, one skilled in the art would need to develop a therapeutic method for treating these diseases by administering statins, or of improving the efficacy of α7-nAChR agonists by co-administering statins. Because there is no evidence either in the prior art or in Applicant's disclosure, suggesting that statins possess any activity against anxiety, Tourette's syndrome, or attention disorders, for example, whether administered alone or in combination with any other agents, the development of this novel therapeutic method would constitute a separate experimental endeavor above and beyond anything disclosed by the Applicant.

In addition to synthesizing candidate compounds and carrying out *in vitro* studies on the molecular target, one skilled in the art wishing to practice the invention using every possible combination would be required to undertake *in vivo* tests in animal models of relevant conditions, such as the ones disclosed in the specification. Animal experiments include, along with the actual induction of disease state, administration of the potential pharmaceutical compound, and collection and analysis of data, additional burdens associated with compliance with animal welfare regulations, care, feeding, and other maintenance of the animals, and disposal of dead animals after the protocol is finished. Human tests involve a similar or greater burden, particularly in recruiting subjects and complying with regulatory and ethical requirements. Because of the unpredictability of the art and the lack of any generalized method for predicting the pharmacological properties of any arbitrarily chosen molecule, these animal experiments would need to be repeated in several different animal models of

Alzheimer's disease, as well as models of Tourette's syndrome, anxiety, depression, schizophrenia, smoking cessation, and Parkinson's disease, and involve the maintenance, killing, and disposal of tens of thousands of experimental animals at minimum, to establish the suitability or lack thereof for each combination found to possess the desired activities *in vitro*.

The sort of unpredictable industrial-scale interdisciplinary drug discovery program described in the preceding paragraphs would present an undue amount of experimentation to require of anyone wishing to practice the invention.

Genentech, 108 F.3d at 1366, sates that, "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion." And "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, in view of the Wands factors, as discussed above, particularly the unpredictability of the art and the lack of working examples, Applicants fail to provide information sufficient to practice the claimed invention for every possible combination of a statin and an α7-nAChR agonist.

Claims 17-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of certain diseases by administering a combination of a statin and an α7-nAChR agonist, does not reasonably provide enablement for prophylaxis against said diseases, here interpreted as prevention according to its ordinary meaning, in any subject at risk thereof by this method. The

specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The Applicant's attention is drawn to *In re Wands*, 8 USPQ2d 1400 (CAFC1988) at 1404 where the court set forth eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) The nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

The Nature of the invention: The claimed invention is a therapeutic method for providing neuroprotection or analgesia for treatment or prophylaxis of one of a number of diseases recited in the claims.

The state of the prior art: The underlying causes of Alzheimer's disease, cognitive and attention disorders, anxiety, depression, schizophrenia, Tourette's syndrome, and Parkinson's disease are not completely understood. No therapies presently exist which are capable of correcting the underlying pathologies associated with these conditions. Rather, existing treatments are directed toward relieving symptoms and slowing progressive damage in order to preserve the patient's condition. Thus prevention or cure of these conditions is not a recognized therapeutic endpoint for any therapy described in the prior art. Kedar (Reference included with PTO-892) discloses that no

preventive or long-term treatment strategies for Alzheimer's or Parkinson's disease are available. (p. 236, left column, first paragraph, p. 237, left column, first paragraph)

In vitro studies have suggested that α7-nAChR agonists may be useful for the inhibition of neural degeneration caused by amyloid peptide. However, there is no reason to believe, based on the prior art, that this therapeutic effect would permanently prevent the onset of cognitive decline in the face of increasing amounts of amyloid peptide accumulating in the subject's brain, as opposed to merely delaying its onset. Similarly, although the incidence of Alzheimer's disease is known to be lower in patients taking statins, there is no evidence that statins are capable of preventing all occurrence of Alzheimer's disease indefinitely.

The relative skill of those in the art: The relative skill of those in the art is high, with a typical practitioner having obtained a PhD or equivalent advanced degree.

The predictability or unpredictability of the art: Prevention of a disease is not the same as treatment of said disease. In order to prevent a disease, as opposed to merely delaying or reducing its symptoms, a treatment must either render the subject completely resistant to said disease after a single treatment or a limited number of treatments, or else, when continued indefinitely, continue to completely suppress the occurrence of said disease. In order to practice a preventative method, one of skill in the art must know the answer to several questions in addition to the effectiveness of the therapy in short-term relief of symptoms, including:

1) What is the duration of a single course of therapy? How often must the therapy be administered to completely suppress the disease?

2) Does the subject develop tolerance to the therapy over time? Does the disease eventually progress to a point where the therapy is unable to completely suppress all symptoms?

3) What are the long-term effects of the therapy? Does it cause progressive damage to the kidneys, liver, or other organs? Does the active agent accumulate in the subject's tissues? Is the minimum dose necessary to completely prevent the disease safe for long-term administration? Are there any steps that can be taken to reduce side effects?

For this reason, many therapies which are suitable for short-term relief of symptoms are not suitable for lifelong prevention of disease. For example, antibiotics, chemotherapeutics, and antiviral drugs are not normally administered to healthy subjects in order to prevent the development of infection or cancer.

Additionally, in order to fully prevent a degenerative disease such as Alzheimer's or Parkinson's disease, degeneration must be stopped completely rather than merely slowed, as the gradual accumulation of irreversible damage, even slowly, will eventually lead to the emergence of a disease state.

The Breadth of the claims: Prevention or prophylaxis is interpreted to indicate a method of eliminating the risk of a disease through an intervention before any symptoms have developed. Prevention can be carried out either by a discrete therapeutic intervention which removes the underlying cause of a disease or renders the subject resistant to the disease, or by an ongoing, lifelong therapeutic regimen which, when adhered to, completely suppresses any manifestation of the disease.

Therapy administered in response to clinical symptoms is not considered to be preventative, as the patient's condition has already manifested itself and is being treated or reversed rather than prevented.

The amount of direction or guidance presented: All the therapeutic methods disclosed or cited by the Applicant involve pharmaceutical compositions not used for therapy prior to Applicant's disclosure. As the average human lifespan is between seventy and eighty years, the Applicant, or any other physician or researcher, could not have observed the long-term efficacy, or lack thereof, of the claimed therapeutic methods. Rather than claiming an actual invention, the term "prevention" merely denotes a hope or prediction. The specification fails to address this concern or give any rationale as to why the disclosed treatment would be expected to be useful for prevention of disease. One practicing the claimed therapeutic method for prevention of diseases associated with reduced cholinergic function would have no guidance from the specification, and would face an undue experimental burden in developing said method. Thus the prevention of diseases associated with reduced cholinergic function is not supported or enabled by the specification.

The presence or absence of working examples: No working examples are presented demonstrating the success of this therapy for the treatment of the claimed diseases, either in the short or long term. The specification is based on extrapolation from the prior art and speculation as to potential therapeutic usefulness of the claimed invention.

Note that lack of working examples is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art such as the treatment of Alzheimer's disease. See MPEP 2164.

The quantity of experimentation necessary: As mentioned above, the short-term usefulness of a therapy for relief of symptoms is no guarantee of its long-term usefulness for prevention of disease. Because no guidance is given for the use of the claimed therapeutic method for the long-term prevention of disease, one skilled in the art wishing to practice the invention would be unable to do so without first gathering information as to the long-term effectiveness of the therapy.

In particular, one skilled in the art would need to know whether the regular administration of nicotinic acetylcholine agonists over a period of decades would adversely affect the health of the subject, in order to determine the maximum safe dose for chronic use and to devise measures to be taken to reduce any side-effects.

Additionally, one skilled in the art, in order to practice the invention for prevention of disease, would need to know whether the preventative effect remains potent over the long term. This is especially true if the method is used to treat a progressive disease such as Alzheimer's disease which is expected to ultimately progress to a state in which no therapy can completely suppress the destructive effects of the amyloid protein. Unless the therapy completely suppress all effects of amyloid protein, or better yet prevents it from being produced in the first place, even a modest rate of accumulation would eventually cause a subject to develop symptoms of the disease in spite of the therapy.

In order to answer these questions in the absence of any existing data, one skilled in the art, in order to practice the invention, would undertake long-term animal tests, preferably over a period of years, preferably involving a relatively long-lived experimental animal such as dogs. Accomplishing this task for each disease included within the claim language would require a suitable animal model for each disease studied, and would need to be repeated for each class of therapeutic compounds studied. Given the number of diseases and compounds included within the claim language, a representative sample would easily involve thousands of experimental animals. Animal experiments include, along with induction of the disease state, administration of the potential pharmaceutical compound and collection and analysis of data, additional burdens associated with compliance with animal welfare regulations, care, feeding, and other maintenance of the animals, dissection of dead animals to collect data, and disposal of dead animals after the protocol is finished. Administering every one of the claimed combinations to tens of thousands of thousands of diseased dogs for a period of years is an undue amount of experimentation needed in order to practice the full range of the claimed invention.

Genentech, 108 F.3d at 1366, sates that, "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion." And "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, in view of the Wands factors, as discussed above, especially the breadth of the claims, the unpredictability of the art, and the lack of guidance or working

examples, Applicants fail to provide information sufficient to practice the claimed invention for the prevention of disease.

Claim Rejections – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 13, 14, 16-20 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Phillips et al. (US patent 6110914, cited in PTO-1449) in view of Jick et al. (Reference included with PTO-1449) Philips et al. discloses a number of α7-nAChR agonists which are useful as therapeutics for the treatment of a number of disorders including Alzheimer's disease. (column 17, line 58 – column 18, line 16) Specific embodiments include a number of compounds, (listed in column 3, line 15 – column 4 line 41, and also in claim 8) all of which are described in instant claim 14 as being useful in the claimed combinations. Phillips et al. does not disclose a combination of any one of said compounds with a statin.

Jick et al. discloses that subjects who were taking statins in order to reduce cholesterol experienced a statistically significant reduction in their incidence of dementia such as Alzheimer's disease. (p. 1629, right column) This effect was determined to be independent of external factors such as the patients' lipid levels.

It would have been obvious to one of ordinary skill in the art to modify the invention of Philips et al. by combining the compounds of Philips et al. with a statin to produce the combinations described by instant claims 13, 14, and 16 and by administering the combination to a patient suffering from Alzheimer's disease as described by instant claims 17-20 and 22. One of ordinary skill in the art would have been motivated to produce this combination in order to provide an effective pharmaceutical composition for the treatment of Alzheimer's disease. One of ordinary skill in the art would reasonably have expected success because both compounds were known individually to be useful for the treatment of Alzheimer's disease.

It has been held that it is *prima facie* obvious to combine two compositions, each of which is taught by the prior art to be useful for the same purpose in order to practice a third composition for the very same purpose. The idea of combining them flows logically from their having been taught individually in the prior art. See *In re Kerkhoven*, 205 USPQ 1069, CCPA 1980.

Thus the invention taken as a whole is *prima facie* obvious.

Allowable Subject Matter

Claim 15 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

The following is the examiner's statement of reasons for allowance: Claim 15 is drawn to a composition of two compounds, both of which are deemed to be enabled by

Applicant's disclosure and cited references. The particular α7-nAChR agonists recited by this claim, namely **spiro[1-azabicyclo[2.2.2]octane-3,5'-oxizolidine]-2'-one** and **(2'R)-5'-(3-furanyl)spiro[1-azabicyclo[2.2.2]octane-3,2'-(3'H)-furo[2,3-b]pyridine]**, are not taught or suggested by the prior art in combination with any statins. Therefore a combination of a statin with one of these compounds is not seen to be anticipated by, or obvious over, the cited prior art as discussed above.

Summary

Claim 15 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. No other claims are allowed in this application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. Olson whose telephone number is 571-272-9051. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571)272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Eric Olson
Patent Examiner
AU 1623
6/19/06

Anna Jiang
6/22/06
Supervisory Patent Examiner
AU 1623